

Amendments to the Claims

This listing of claims will replace all prior versions and listings of all claims in the application.

Claims

1. (Currently Amended) A polypeptide comprising an Fc variant comprising at least one amino acid modification in the Fc region of a parent polypeptide, wherein said Fc variant comprises at least one substitution at a position selected from the group consisting of: 234, 239, 240, 241, 243, 244, 245, 247, 262, 263, 264, 266, 299, 313, 325, 327, 328, and 332, wherein numbering is according to the EU Index, and wherein said Fc variant ~~modulates~~ increases binding affinity to an Fc γ R as compared to said parent polypeptide.
2. (Currently Amended) The polypeptide according to claim 1, wherein said substitution is at the position 239A~~polypeptide according to claim 1 wherein said modulation is an increase in affinity of said antibody to said Fc γ R.~~
3. (Currently Amended) A polypeptide according to claim [[1]] 2, wherein said substitution is 239D~~Fc variant comprises at least one substitution at a position selected from the group consisting of: 234, 235, 239, 240, 241, 243, 244, 245, 247, 262, 263, 264, 265, 266, 267, 268, 269, 296, 297, 299, 313, 325, 326, 327, 328, 329, 330, and 332, wherein numbering is according to the EU Index.~~
4. (Cancelled)
5. (Withdrawn – Currently Amended) A polypeptide according to claim 1, wherein said Fc variant comprises a substitution at position 332,~~wherein numbering is according to the EU Index.~~
6. (Currently Amended) A polypeptide according to claim 1, wherein at least one substitution is at a position selected from the group consisting of: 239, 264, 297, and 330, with the proviso that if said sequence is substantially human, said substitution is not S239A, V264A, N297A, N297Q, A330D, A330Q, A330K, or A330S,~~wherein numbering is according to the EU Index.~~
7. (Currently Amended) A polypeptide according to claim 1, wherein said Fc variant comprises at least one substitution selected from the group consisting of 234D, 234E, 234N, 234Q, 234T, 234H, 234Y, 234I, 234V, 234F, ~~235D, 235S, 235N, 235Q, 235T, 235H, 235Y, 235I, 235V, 235F, 239D, 239E, 239N, 239Q, 239F, 239T, 239H, 239Y, 240I, 240A, 240T, 240M, 241W, 241L, 241Y, 241E, 241R, 243W, 243L, 243Y, 243R, 243Q, 244H, 245A, 247V, 247G, 262I, 262A, 262T, 262E, 263I, 263A, 263T, 263M, 264L, 264I, 264W, 264T, 264R, 264F, 264M, 264Y, 264E, 265G, 265N, 265Q, 265Y, 265F, 265V, 265I, 265L, 265H,~~

265T, 266I, 266A, 266T, 266M, 267Q, 267L, 269H, 269Y, 269F, 269R, 296E, 296Q, 296D, 296N, 296S, 296T, 296L, 296I, 296H, 297S, 297D, 297E, 298H, 299I, 299L, 299A, 299S, 299V, 299H, 299F, 299E, 313F, 325Q, 325L, 325I, 325D, 325E, 325A, 325T, 325V, 325H, 327N, 327L, 328M, 328D, 328E, 328N, 328Q, 328F, 328I, 328V, 328T, 328H, 328A, 329F, 330L, 330Y, 330V, 330I, 330F, 330R, 330H, 332D, 332E, 332N, 332Q, 332T, 332H, 332Y, and 332A, wherein numbering is according to the EU Index.

8. (Withdrawn – Currently Amended) A polypeptide according to claim 1, wherein said Fc variant is selected from the group consisting of 264L, 264I, 241W, 241L, 243W, 243L, 241L/243L/262I/264I, 241W/243W, 241W/243W/262A/264A, 241L/262I, 243L/264I, 243L/262I/264W, 241Y/243Y/262T/264T, 241E/243R/262E/264R, 241E/243Q/262T/264E, 241R/243Q/262T/264R, 241E/243Y/262T/264R, 328M, 328E, 328F, 332E, 328M/332E, 244H, 245A, 247V, 313F, 244H/245A/247V, 247G, 264I/332E, 241E/243R/262E/264R/332E, 241E/243Q/262T/264E/332E, 241R/243Q/262T/264R/332E, 241E/243Y/262T/264R/332E, 298A/332E, 239E/332E, 239Q/332E, 239E, 265G, 265N, 239E/265G, 239E/265N, 239E/265Q, 296E, 296Q, 299I, 327N, 267Q/327S, 267L/327S, 327L, 329F, 330L, 330Y, 332D, 297S, 297D, 297S/332E, 297D/332E, 297E/332E, 265Y/297D/332E, 265Y/297D/299L/332E, 265F/297E/332E, 328I/332E, 328Q/332E, 332N, 332Q, 264T, 264F, 240I, 263I, 266I, 299A, 299S, 299V, 325Q, 325L, 325I, 239D, 239N, 239F, 239D/332D, 239D/332E, 239D/332N, 239D/332Q, 239E/332D, 239E/332N, 239E/332Q, 239N/332D, 239N/332E, 239N/332N, 239N/332Q/239N/332Q, 239Q/332D, 239Q/332N, 239Q/332Q, 296D, 296N, 241Y/243Y/262T/264T/297D/332E, 330Y/332E, 264I/330Y/332E, 330L/332E, 264I/330L/332E, 234D, 234E, 234N, 234Q, 234T, 234H, 234Y, 234I, 234V, 234F, 235D, 235S, 235N, 235Q, 235T, 235H, 235Y, 235I, 235V, 235F, 239T, 239H, 239Y, 240A, 240T, 240M, 263A, 263T, 263M, 264M, 264Y, 266A, 266T, 266M, 269H, 269Y, 269F, 269R, 296S, 296T, 296L, 296I, 298H, 299H, 330V, 330I, 330F, 330R, 330H, 325D, 325E, 325A, 325T, 325V, 325H, 328D/332E, 328E/332E, 328N/332E, 328Q/332E, 328V/332E, 328T/332E, 328H/332E, 328I/332E, 328A, 332T, 332H, 332Y, 332A, 239E/264I/332E, 239Q/264I/332E, 239E/264I/330Y/332E, 239E/264I/298A/330Y/332E, 239D/297D/332E, 239E/297D/332E, 239D/265V/297D/332E, 239D/265I/297D/332E, 239D/265L/297D/332E, 239D/265F/297D/332E, 239D/265Y/297D/332E, 239D/265H/297D/332E, 239D/265T/297D/332E, 264E/297D/332E, 296D/297D/332E, 296E/297D/332E, 296N/297D/332E, 296Q/297D/332E, 296H/297D/332E, 296T/297D/332E, 297D/299V/332E, 297D/299I/332E, 297D/299L/332E, 297D/299F/332E, 297D/299H/332E, 297D/299E/332E, 297D/330Y/332E, 297D/298A/330Y/332E, 297D/298A/330Y/332E, 239D/330Y/332E, 239N/330Y/332E, 239D/330L/332E, 239N/330L/332E, 264I/298A/332E, 239D/298A/332E, 239N/298A/332E, 239D/264I/332E, 239D/264I/298A/332E, and 239D/264I/330L/332E, wherein numbering is according to the EU Index.

9. (Withdrawn) A polypeptide according to claim 7, wherein said Fc variant further comprises at least one substitution selected from the group consisting of: 256, 270, 290, 298, 312, 322, 326, 329, 331, 333, 334, and 339.

10. (Previously Presented) A polypeptide according to claim 1, wherein said FcγR is FcγRIIIa.

11. (Previously Presented) A polypeptide according to claim 10, wherein said FcγRIIIa is a V158 or F158 allotype of FcγRIIIa.

12. (Currently Amended) A polypeptide according to claim ~~[[2]]~~ 1, wherein said parent polypeptide is substantially-human, and said affinity of said Fc variant is approximately 5-fold greater than that of said parent polypeptide.

13. (Currently Amended) A polypeptide according to claim 12, wherein said parent polypeptide is substantially-human, and said affinity of said Fc variant is between about 5-fold and about 300-fold greater than that of said parent polypeptide.

14. (Currently Amended) A polypeptide according to claim ~~[[12]]~~ 1, wherein said Fc variant ~~portion~~ comprises at least one substitution selected from the group consisting of 234, ~~235~~, 239, 240, 243, 264, 266, 268, ~~328~~, ~~330~~, 325, 327, 328, 332, and 325, ~~wherein numbering is according to the EU Index.~~

15. (Previously Presented) A polypeptide according to claim 14, wherein said Fc variant comprises at least one substitution selected from the group consisting of ~~234E~~, 234N, 234Y, 234I, ~~235D~~, ~~235S~~, ~~235Y~~, ~~235I~~, ~~239D~~, ~~239E~~, 239N, 239Q, 239T, 240I, 240M, 243L, 264I, 264T, 264Y, 266I, ~~268D~~, ~~268E~~, 327N, 328M, 328I, 328Q, 328D, 328V, 328T, 328M, ~~330Y~~, ~~330L~~, ~~330I~~, 332D, 332E, 332N, 332Q, and 325T.

16. (Previously Presented) A polypeptide according to claim 15, wherein said Fc variant is selected from the group consisting of 264I, 243L/264I, 328M, 332E, 328M/332E, 264I/332E, 298A/332E, 239E/332E, 239Q/332E, 239E, ~~330Y~~, 332D, 328I/332E, 328Q/332E, 264T, 240I, 266I, 239D, 239D/332D, 239D/332E, 239D/332N, 239D/332Q, 239E/332D, 239E/332N, 239E/332Q, 239N/332D, 239N/332E, 239Q/332D, 330Y/332E, 264I/330Y/332E, 330L/332E, 264I/330L/332E, ~~234E~~, 234Y, 234I, ~~235D~~, ~~235S~~, ~~235Y~~, ~~235I~~, 239T, 240M, 264Y, ~~330I~~, 325T, ~~268D~~, ~~268E~~, 328D/332E, 328V/332E, 328T/332E, 328I/332E, 239E/264I/332E, 239Q/264I/332E, 239E/264I/330Y/332E, 239D/330Y/332E, 239N/330Y/332E, 239D/330L/332E, 239N/330L/332E, 264I/298A/332E, 239D/298A/332E, 239N/298A/332E, 239D/264I/332E, 239D/264I/298A/332E, and 239D/264I/330L/332E.

17. (Withdrawn) A polypeptide according to claim 15, wherein said Fc variant further comprises at least one substitution at a position selected from the group consisting of 235, 256, 268, 270, 290, 298, 312, 322, 326, 327, 328, 329, 331, 333, 334, and 339.

18 (Currently Amended) A polypeptide according to claims 1 or 2, wherein said parent polypeptide is ~~substantially human, substantially mouse, substantially rat, or substantially monkey.~~

19. (Previously Presented) A polypeptide according to claims 1 or 2, wherein binding to one or more Fc ligands is unaltered.

20. (Withdrawn) A polypeptide according to claim 19, wherein said Fc ligand is selected from the group consisting of C1q, FcRn, protein A, and protein G.

21. (Previously Presented) A polypeptide according to claims 1 or 2, wherein CDC is unaffected.

22. (Previously Presented) A polypeptide according to claims 1 or 2, wherein binding to one or more Fc ligands is altered.

23. (Previously Presented) A polypeptide according to claim 1, wherein said Fc variant has a FcγRIIIa-fold:FcγRIIb-fold ratio greater than 1.

24. (Previously Presented) A polypeptide according to claim 23, wherein said Fc variant has a FcγRIIIa-fold:FcγRIIb-fold ratio greater than approximately 11:1.

25. (Previously Presented) A polypeptide according to claim 24, wherein said Fc variant has a FcγRIIIa-fold:FcγRIIb-fold ratio between approximately 11:1 and approximately 86:1.

26. (Currently Amended) A polypeptide according to claim 23, wherein said Fc variant comprises at least one substitution at a position selected from the group consisting of: 234, 235, 239, 240, 264, ~~268~~, ~~296~~, ~~330~~, and ~~332~~ 332, ~~wherein numbering is according to the EU Index.~~

27. (Previously Presented) A polypeptide according to claim 26, wherein said Fc variant comprises at least one substitution selected from the group consisting of: 234Y, 234I, ~~235I~~, 239D, 239E, 239N, 239Q, 240A, 240M, 264I, 264Y, ~~296Q, 268D, 268E, 330L, 330Y, 330I~~, 332D, and 332E.

28. (Previously Presented) A polypeptide according to claim 27, wherein said Fc variant is selected from the group consisting of 332E, 264I/332E, 239E/332E, 239Q/332E, ~~296Q, 330L, 330Y~~, 332D, 239D, 239D/332E, 330Y/332E, 264I/330Y/332E, 330L/332E, 264I/330L/332E, 234Y, 234I, ~~235I~~, 240A, 240M, 264Y, 330I, 239D/330L/332E, 239D/298A/332E, 239N/298A/332E, 239D/264I/332E, 239D/264I/298A/332E, and 239D/264I/330L/332E.

29. (Withdrawn) A polypeptide according to claim 26, wherein said Fc variant further comprises one or more substitutions at a position selected from the group consisting of 235, 256, 268, 270, 290, 296, 298, 312, 322, 326, 329, 330, 331, 333, 334, and 339.

30. (Withdrawn) A polypeptide according to claim 1, wherein said Fc variant binds to at least one FcγR with reduced affinity relative to said parent polypeptide.

31. (Withdrawn) A polypeptide according to claim 30, wherein said FcγR is FcγRIIIa.

32. (Withdrawn – Currently Amended) A polypeptide according to claim 31, wherein said Fc variant comprises at least one substitution selected from the group consisting of 234D, 234N, 234Q, 234T, 234H, 234V, 234F, 235N, 235Q, 235T, 235H, 235V, 235F, 239E, 239N, 239Q, 239F, 239H, 239Y, 240A, 240T, 241W, 241L, 241Y, 241E, 241R, 243W, 243L, 243Y, 243R, 243Q, 244H, 245A, 247V, 247G, 262I, 262A, 262T, 262E, 263I, 263A, 263T, 263M, 264L, 264I, 264W, 264T, 264R, 264F, 264M, 264E, 265G, 265N, 265Q, 265Y, 265F, 265V, 265I, 265L, 265H, 265T, 266A, 266T, 266M, 267Q, 267L, 269H, 269Y, 269F, 269R, 296E, 296Q, 296D, 296N, 296S, 296T, 296L, 296I, 296H, 297S, 297D, 297E, 298H, 299I, 299L, 299A, 299S, 299V, 299H, 299F, 299E, 313F, 325Q, 325L, 325I, 325D, 325E, 325A, 325V, 325H, 327N, 327L, 328M, 328E, 328N, 328Q, 328F, 328H, 328A, 329F, 330L, 330V, 330F, 330R, 330H, 332N, 332Q, 332T, 332H, 332Y, and 332A, ~~wherein numbering is according to the EU Index.~~

33. (Withdrawn – Currently Amended) A polypeptide according to claim 31, wherein said Fc variant is selected from the group consisting of 264L, 241W, 241L, 243W, 243L, 241L/243L/262I/264I, 241W/243W, 241W/243W/262A/264A, 241L/262I, 243L/262I/264W, 241Y/243Y/262T/264T,

241E/243R/262E/264R, 241E/243Q/262T/264E, 241R/243Q/262T/264R, 241E/243Y/262T/264R, 328M, 328E, 328F, 244H, 245A, 247V, 313F, 244H/245A/247V, 247G, 241E/243R/262E/264R/332E, 241E/243Y/262T/264R/332E, 265G, 265N, 239E/265G, 239E/265N, 239E/265Q, 296E, 296Q, 299I, 327N, 267Q/327S, 267L/327S, 327L, 329F, 330L, 297S, 297D, 297S/332E, 332N, 332Q, 264F, 263I, 299A, 299S, 299V, 325Q, 325L, 325I, 239N, 239F, 239N/332N, 239N/332Q, 239Q/332N, 239Q/332Q, 296D, 296N, 234D, 234N, 234Q, 234T, 234H, 234V, 234F, 235N, 235Q, 235T, 235H, 235V, 235F, 239H, 239Y, 240A, 263T, 263M, 264M, 266A, 266T, 266M, 269H, 269Y, 269F, 269R, 296S, 296T, 296L, 296I, 298H, 299H, 330V, 330F, 330R, 330H, 325D, 325E, 325A, 325V, 325H, 328E/332E, 328N/332E, 328Q/332E, 328H/332E, 328A, 332T, 332H, 332Y, and 332A, ~~wherein numbering is according to the EU Index.~~

34. (Currently Amended) A polypeptide comprising an Fc variant comprising at least one amino acid modification in the Fc region of a parent polypeptide, wherein said Fc variant ~~modulates~~ increases effector function ADCC or ADCP as compared to said parent polypeptide, and wherein said Fc variant comprises at least one substitution at a position selected from the group consisting of: 234, 239, 240, 243, 264, 266, 328, 332, and 325, wherein numbering is according to the EU Index.

35. (Withdrawn) A polypeptide according to claim 34, wherein said effector function is ADCC.

36. (Withdrawn) A polypeptide according to claim 35, wherein said Fc variant improves ADCC as compared to said parent polypeptide.

37. (Withdrawn) A polypeptide according to claim 36, wherein said ADCC improvement is approximately 5-fold greater than that of said parent polypeptide.

38. (Withdrawn) A polypeptide according to claim 37, wherein said ADCC improvement is between approximately 5-fold and 50-fold greater than that of said parent polypeptide.

39. (Cancelled)

40. (Currently Amended) A polypeptide according to claim ~~39~~ 34, wherein said Fc variant comprises at least one substitution selected from the group consisting of 234E, 234Y, 234I, ~~235D, 235S, 235Y, 235I,~~

239D, 239E, 239N, 239Q, 239T, 240I, 240M, 243L, 264I, 264T, 264Y, 266I, 328M, 328I, 328Q, 328D, 328V, 328T, ~~330Y, 330L, 330I, 332D, 332E, 332N, 332Q, and 325T.~~

41. (Currently Amended) A polypeptide according to claim 39, wherein said Fc variant is selected from the group consisting of 264I, 243L/264I, 328M, 332E, 328M/332E, 264I/332E, 298A/332E, 239E/332E, 239Q/332E, 239E, ~~330Y, 332D, 328I/332E, 328Q/332E, 264T, 240I, 266I, 239D, 239D/332D, 239D/332E, 239D/332N, 239D/332Q, 239E/332D, 239E/332N, 239E/332Q, 239N/332D, 239N/332E, 239Q/332D, 330Y/332E, 264I/330Y/332E, 330L/332E, 264I/330L/332E, 234E, 234Y, 234I, 235D, 235S, 235Y, 235I, 239T, 240M, 264Y, 330I, 325T, 328D/332E, 328V/332E, 328T/332E, 328I/332E, 239E/264I/332E, 239Q/264I/332E, 239E/264I/330Y/332E, 239D/330Y/332E, 239N/330Y/332E, 239D/330L/332E, 239N/330L/332E, 264I/298A/332E, 239D/298A/332E, 239N/298A/332E, 239D/264I/332E, 239D/264I/298A/332E, and 239D/264I/330L/332E.~~

42. (Withdrawn) A polypeptide according to claim ~~34~~39, wherein said Fc variant further comprises at least one substitution at a position selected from the group consisting of 256, 270, 290, 298, 312, 322, 326, 329, 331, 333, 334, and 339.

43. (Withdrawn – Currently Amended) A polypeptide according to claim ~~34~~39, wherein said parent polypeptide is ~~substantially-human, substantially-mouse, substantially-rat, or substantially-monkey.~~

44. (Withdrawn) A polypeptide according to claim 35, wherein said Fc variant reduces ADCC as compared to said parent polypeptide.

45. (Currently Amended - Withdrawn) A polypeptide according to claim 44, wherein said Fc variant comprises at least one substitution selected from the group consisting of 234D, 234N, 234Q, 234T, 234H, 234V, 234F, 235N, 235Q, ~~235T, 235H, 235V, 235F, 239E, 239N, 239Q, 239F, 239H, 239Y, 240A, 240T, 241W, 241L, 241Y, 241E, 241R, 243W, 243L 243Y, 243R, 243Q, 244H, 245A, 247V, 247G, 262I, 262A, 262T, 262E, 263I, 263A, 263T, 263M, 264L, 264I, 264W, 264T, 264R, 264F, 264M, 264E, 265G, 265N, 265Q, 265Y, 265F, 265V, 265I, 265L, 265H, 265T, 266A, 266T, 266M, 267Q, 267L, 269H, 269Y, 269F, 269R, 296E, 296Q, 296D, 296N, 296S, 296T, 296L, 296I, 296H, 297S, 297D, 297E, 298H, 299I, 299L, 299A, 299S, 299V, 299H, 299F, 299E, 313F, 325Q, 325L, 325I, 325D, 325E, 325A, 325V, 325H, 327N, 327L, 328M, 328E, 328N, 328Q, 328F, 328H, 328A, 329F, 330L, 330V, 330F, 330R, 330H, 332N, 332Q, 332T, 332H, 332Y, and 332A, wherein numbering is according to the EU Index.~~

46. (Currently Amended - Withdrawn) A polypeptide according to claim 44, wherein said Fc variant is selected from the group consisting of 264L, 241W, ~~241L~~, 243W, 243L, 241L/243L/262I/264I, 241W/243W, 241W/243W/262A/264A, ~~241L/262I~~, 243L/262I/264W, 241Y/243Y/262T/264T, 241E/243R/262E/264R, 241E/243Q/262T/264E, 241R/243Q/262T/264R, 241E/243Y/262T/264R, 328M, 328E, 328F, ~~244H~~, ~~245A~~, ~~247V~~, ~~313F~~, ~~244H/245A/247V~~, ~~247G~~, 241E/243R/262E/264R/332E, 241E/243Y/262T/264R/332E, ~~265G~~, ~~265N~~, 239E/265G, 239E/265N, 239E/265Q, ~~296E~~, ~~296Q~~, ~~299I~~, 327N, ~~267Q/327S~~, ~~267L/327S~~, ~~327L~~, ~~329F~~, ~~330L~~, ~~297S~~, ~~297D~~, 297S/332E, 332N, 332Q, 264F, ~~263I~~, 299A, 299S, 299V, 325Q, 325L, 325I, 239N, 239F, 239N/332N, 239N/332Q, 239Q/332N, 239Q/332Q, 296D, 296N, 234D, 234N, 234Q, 234T, 234H, 234V, 234F, ~~235N~~, ~~235Q~~, ~~235T~~, ~~235H~~, ~~235V~~, ~~235F~~, 239H, 239Y, 240A, ~~263T~~, ~~263M~~, 264M, 266A, 266T, 266M, ~~269H~~, ~~269Y~~, ~~269F~~, ~~269R~~, ~~296S~~, ~~296T~~, ~~296L~~, ~~296I~~, ~~298H~~, ~~299H~~, ~~330V~~, ~~330F~~, ~~330R~~, ~~330H~~, 325D, 325E, 325A, 325V, 325H, 328E/332E, 328N/332E, 328Q/332E, 328H/332E, 328A, 332T, 332H, 332Y, and 332A, ~~wherein numbering is according to the EU Index.~~

47. (Currently Amended) A polypeptide comprising an aglycosylated Fc variant of a parent polypeptide comprising at least one amino acid modification in the Fc region of said parent polypeptide, wherein said aglycosylated Fc variant has improved stability, solubility, or binding affinity to an Fc ligand relative to the aglycosylated form of said parent polypeptide, and wherein said modification is at a position selected from the group consisting of 239, 241, 243, 262, 264, and 332, wherein numbering is according to the EU Index.

48. (Previously Presented) A polypeptide according to claim 47, wherein said aglycosylated Fc variant has improved binding affinity to an Fc ligand as compared to the aglycosylated form of said parent polypeptide.

49. (Previously Presented) A polypeptide according to claim 48, wherein said Fc ligand is an FcγR.

50. (Previously Presented) A polypeptide according to claim 49, wherein said FcγR is FcγRIIIa.

51. (Previously Presented) A polypeptide according to claim 48, wherein said improved binding affinity is within 0.4-fold of the glycosylated form of said parent polypeptide.

52. (Cancelled)

53. (Previously Presented) A polypeptide according to claim 52, wherein said Fc variant comprises one or more substitutions selected from the group consisting of 239D, 239E, 241Y, 243Y, 262T, 264T, 264E, 265Y, 265H, 268D, 268E, 296N, 297D, 330Y, and 332E.

54. (Previously Presented) A polypeptide according to claim 52, wherein said Fc variant is selected from the group consisting of 297D/332E, 241Y/243Y/262T/264T/297D/332E, 239D/297D/332E, 239E/297D/332E, 239D/265Y/297D/332E, 239D/265H/297D/332E, 264E/297D/332E, 296N/297D/332E, and 297D/330Y/332E.

55. (Withdrawn – Currently Amended) A polypeptide according to claim ~~47~~[[52]], wherein said aglycosylated Fc variant further comprises at least one substitution selected from the group consisting of: 256, 270, 290, 298, 312, 322, 326, 329, 331, 333, 334, and 339, ~~wherein numbering is according to the EU Index.~~

56. (Cancelled)

57. (Currently Amended) A polypeptide according to claim 1, wherein said ~~antibody~~ polypeptide further comprises an engineered glycoform.

58. (Previously Presented) A polypeptide according to claim 57, wherein said engineered glycoform improves effector function.

59. (Previously Presented) A pharmaceutical composition comprising a polypeptide according to claim 1 and a pharmaceutically acceptable carrier.

60. (Cancelled)

61. (Withdrawn – Currently Amended) An antibody comprising an Fc variant, said Fc variant comprising at least one substitution selected from the group consisting of: 332D, 332E, 332N, and 332Q, wherein said antibody has specificity for a target antigen selected from the group consisting of CD4, CD19, CD20, CD22, CD25, CD30, CD33, CD52, CD80, B7-1, B7-2, CTLA-4, BAFF-R, Her2/neu, EGFR, EpCAM,

MUC1, GD3, CEA, CA 125, HLA-DR, TNFalpha, and VEGF, ~~wherein numbering is according to the EU Index.~~

62. (Withdrawn – Currently Amended) An antibody comprising an Fc variant, said Fc variant comprising at least one substitution selected from the group consisting of 264I, 264T, and 264Y, wherein said antibody has specificity for a target antigen selected from the group consisting of CD4, CD19, CD20, CD22, CD25, CD30, CD33, CD52, CD80, B7-1, B7-2, CTLA-4, BAFF-R, Her2/neu, EGFR, EpCAM, MUC1, GD3, CEA, CA 125, HLA-DR, TNFalpha, and VEGF, ~~wherein numbering is according to the EU Index.~~

63. (Currently Amended) An antibody comprising an Fc variant, said Fc variant comprising at least one substitution selected from the group consisting of 239D, 239E, 239N, 239Q, and 239T, wherein said antibody has specificity for a target antigen selected from the group consisting of CD4, CD19, CD20, CD22, CD25, CD30, CD33, CD52, CD80, B7-1, B7-2, CTLA-4, BAFF-R, Her2/neu, EGFR, EpCAM, MUC1, GD3, CEA, CA 125, HLA-DR, TNFalpha, and VEGF, ~~wherein numbering is according to the EU Index.~~

64. (Cancelled)

65. (Withdrawn – Currently Amended) An antibody comprising an Fc variant, said Fc variant comprising at least one substitution selected from 240I or 240M, wherein said antibody has specificity for a target antigen selected from the group consisting of CD4, CD19, CD20, CD22, CD25, CD30, CD33, CD52, CD80, B7-1, B7-2, CTLA-4, BAFF-R, Her2/neu, EGFR, EpCAM, MUC1, GD3, CEA, CA 125, HLA-DR, TNFalpha, and VEGF, ~~wherein numbering is according to the EU Index.~~

66. (Cancelled)

67. (Withdrawn – Currently Amended) An antibody according to claim 61, 62, 63, 64, ~~or 65 or 66~~ wherein said Fc variant additionally comprises the substitution 298A.

68. (Withdrawn – Currently Amended) An antibody according to claim 61, 62, 63, 64, ~~or 65, or 66~~ wherein said Fc variant additionally comprises the substitution 333A or 334A.

69. (Withdrawn – Currently Amended) An antibody variant of a parent antibody, said antibody variant comprising two or more amino acid modifications in the Fc region of said parent antibody, wherein said

antibody variant has improved ADCC in the presence of human effector cells as compared to wild type IgG1.

70. (Withdrawn) An antibody according to claim 69, wherein said Fc region is a human IgG Fc region.

71. (Withdrawn) An antibody according to claim 70, wherein said Fc region is a human IgG1 Fc region.

72. (Withdrawn) An antibody according to claim 70, wherein said Fc region is a human IgG2 Fc region.

73. (Withdrawn) An antibody according to claim 70, wherein said Fc region is a human IgG3 Fc region.

74. (Withdrawn) An antibody according to claim 70, wherein said Fc region is a human IgG4 Fc region.

75. (Withdrawn) A polypeptide according to claim 36, wherein said Fc variant comprises the substitution 298A and at least one additional substitution selected from E333A or K334A, wherein numbering is according to the EU Index, and wherein said polypeptide binds to CD20.

76. (Withdrawn) A polypeptide according to claim 75, wherein said Fc variant comprises the substitutions 298A, E333A and K334A.

77. (Withdrawn) A polypeptide according to claim 75, wherein said Fc variant comprises an additional substitution at position 326.

78. (Withdrawn) A polypeptide according to claim 36, wherein said Fc variant comprises the substitutions 298A, 333A and 334A, wherein numbering is according to the EU index and wherein said ADCC is against CD20 bearing cells.

79. (Previously Presented) A polypeptide according to claim 1, wherein said Fc variant comprises either increased binding to an Fc γ R or enhanced ADCC, as compared to a parent antibody.

80. (Previously Presented) A polypeptide according to claim 79, wherein said Fc variant comprises increased binding to an Fc γ R and enhanced ADCC, as compared to a parent antibody.

81. (Withdrawn) A polypeptide according to claim 80, wherein said Fc variant comprises at least two amino acid modifications.

82. (Withdrawn – Currently Amended) A polypeptide according to claim ~~[[3]]~~1, wherein said substitution is at position 268 and said substitution is a negatively charged amino acid.

83. (Withdrawn) A polypeptide according to claim 82 wherein said negatively charged amino acid is aspartic acid.

84. (Withdrawn) A polypeptide according to claim 82 wherein said negatively charged amino acid is glutamic acid.

85. (Withdrawn – Currently Amended) An antibody comprising an Fc variant, said Fc variant comprising at least one substitution selected from 268D or 268E, wherein said antibody has specificity for a target antigen selected from the group consisting of CD4, CD19, CD20, CD22, CD25, CD30, CD33, CD52, CD80, B7-1, B7-2, CTLA-4, BAFF-R, Her2/neu, EGFR, EpCAM, MUC1, GD3, CEA, CA 125, HLA-DR, TNFalpha, and VEGF, ~~wherein numbering is according to the EU Index.~~

86. (New) A polypeptide according to claim 1, wherein said Fc variant is an antibody.

87. (New) A polypeptide according to claim 1, wherein said Fc variant is an Fc fusion.